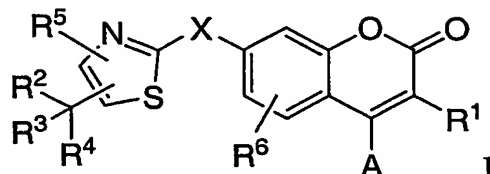


WHAT IS CLAIMED:

1. A compound of structural Formula I



5 and the pharmaceutically acceptable salts and esters thereof wherein:

R¹ is selected from the group consisting of -H, -C₁₋₆ alkyl and -C₃₋₆ cycloalkyl;

R² is selected from the group consisting of -H, -OH, -OC₁₋₃alkyl, -F and tetrazolyl, provided that when R² is tetrazolyl then neither R³ nor R⁴ is Z;

10 R³ is selected from the group consisting of -H, -CF₃, -CF₂CF₃, -C₁₋₆alkyl, -C₁₋₆alkyl substituted with fluoro, -C₁₋₆alkyl-R⁷, -C₂₋₆alkenyl, -C₃₋₆cycloalkyl, -C₅₋₇cycloalkenyl and -Z;

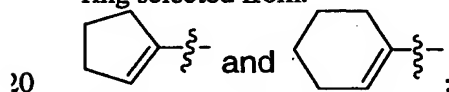
R⁴ is selected from the group consisting of -H, -CF₃, -CF₂CF₃, -C₁₋₆alkyl, -C₁₋₆alkyl substituted with fluoro, -C₁₋₆alkyl-R⁷, -C₂₋₆alkenyl, -C₃₋₆cycloalkyl, -C₅₋₇cycloalkenyl and -Z;

or R³ and R⁴ are joined together with the carbon to which they are attached to form a ring selected from the group consisting of a -C₃₋₆cycloalkyl ring and a -C₅₋₇cycloalkenyl ring, provided that when R³ and

15 R⁴ are joined together with the carbon to which they are attached to form a -C₅₋₇cycloalkenyl ring, there is no double bond at the C1 position in the ring;

or R² and R³ are joined together to form =C₁₋₆alkyl;

or R², R³ and R⁴ are joined together with the carbon to which they are attached to form a cycloalkenyl ring selected from:



R⁵ is selected from the group consisting of -H, -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl and halo;

R⁶ is selected from the group consisting of -H, -C₁₋₆ alkyl, -C₃₋₆ cycloalkyl and halo;

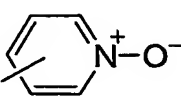
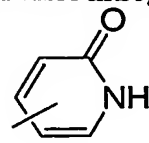
R⁷ is selected from the group consisting of -COOR¹, -C(O)H, -CN, -CR¹R¹OH, -OR¹, -S-C₁₋₆alkyl and -S-C₃₋₆ cycloalkyl;

25 A is selected from the group consisting of

a) a 5-membered aromatic ring containing (i) one or more carbon atoms, (ii) one heteroatom selected from oxygen and sulfur, and (iii) zero, one, two or three nitrogen atoms,

b) a 5-membered aromatic ring containing one or more carbon atoms and from one to four nitrogen atoms,

c) a 6-membered aromatic ring containing carbon atoms and one, two or three nitrogen atoms;

d) a 6-membered aromatic ring selected from  and ,

e) a bicyclic aromatic ring system selected from benzothienyl, indolyl, quinolinyl and naphthalenyl;

f) phenyl,

g) $-\text{CH}_2-\text{R}^8$, wherein R^8 is selected from phenyl and dioxolanyl,

h) $-\text{C}_3\text{-6cycloalkyl}$,

i) $-\text{C}_5\text{-7cycloalkenyl}$,

j) $-\text{C}_1\text{-6alkyl}$; and

k) $-\text{C}_2\text{-6alkenyl}$,

and wherein A is optionally mono- or di-substituted with a substituent independently selected at each occurrence from the group consisting of (i) halo, (ii) $-\text{OH}$, (iii) $-\text{C}_1\text{-3alkyl}$ optionally substituted with one or more of halo, (iv) $-\text{OC}_1\text{-3alkyl}$ optionally substituted with one or more of halo, (v) $-\text{OC}_3\text{-6cycloalkyl}$, (vi) $-\text{CH}_2\text{OH}$, (vii) $-\text{COOR}^1$, (viii) $-\text{CN}$ and (ix) $-\text{NR}^9\text{R}^{10}$;

R^9 is selected from the group consisting of $-\text{H}$, $-\text{C}_1\text{-6 alkyl}$ and $-\text{C}_3\text{-6 cycloalkyl}$;

R^{10} is selected from the group consisting of $-\text{H}$, $-\text{C}_1\text{-6 alkyl}$, $-\text{C}_3\text{-6 cycloalkyl}$ and $-\text{COOR}^1$;

X is selected from the group consisting of $-\text{S}-$, $-\text{SO}-$ and $-\text{SO}_2-$; and

Z is selected from the group consisting of

a) a 5-membered aromatic ring containing (i) one or more carbon atoms, (ii) one heteroatom selected from oxygen and sulfur, and (iii) zero, one, two or three nitrogen atoms,

b) a 5-membered aromatic ring containing one or more carbon atoms and from one to four nitrogen atoms,

c) a 6-membered aromatic ring containing carbon atoms and one, two or three nitrogen atoms;

d) phenyl, and

e) $-\text{CH}_2-\text{R}^8$, wherein R^8 is selected from phenyl and dioxolanyl,

and wherein Z is optionally mono- or di-substituted with a substituent independently selected at each occurrence from the group consisting of (i) halo, (ii) $-\text{OH}$, (iii) $-\text{C}_1\text{-3alkyl}$ optionally substituted with one or more of halo, (iv) $-\text{OC}_1\text{-3alkyl}$ optionally substituted with one or more of halo, (v) $-\text{OC}_3\text{-6cycloalkyl}$, (vi) $-\text{CH}_2\text{OH}$, (vii) $-\text{COOR}^1$, (viii) $-\text{CN}$ and (ix) $-\text{NR}^9\text{R}^{10}$.

2. The compound of claim 1 and the pharmaceutically acceptable salts and esters thereof wherein:

R¹ is selected from -H and -C₁₋₆ alkyl;

R² is selected from the group consisting of -H, -OH and -F;

R³ is selected from the group consisting of -C₁₋₆alkyl optionally substituted with fluoro, -C₁₋₆alkyl-R⁷, and -C₃₋₆cycloalkyl;

5 R⁴ is selected from the group consisting of -C₁₋₆alkyl optionally substituted with fluoro, -C₁₋₆alkyl-R⁷, -C₂₋₆alkenyl, -C₃₋₆cycloalkyl and -Z;

or R³ and R⁴ are joined together with the carbon to which they are attached to form a -C₃₋₆cycloalkyl ring;

R⁵ is selected from -H and -CH₃;

0 R⁶ is selected from the group consisting of -H and -CH₃;

A is unsubstituted, mono- or di-substituted and is selected from the group consisting of:

a) a 5-membered aromatic ring comprised of carbon, one heteroatom selected from -O- and -S-, and zero, one, two or three of -N-,

b) a 5-membered aromatic ring comprised of carbon and from one to four of -N-,

.5 c) a 6-membered aromatic ring comprised of carbon and one, two or three of -N- and

d) phenyl; and

Z is unsubstituted, mono- or di-substituted and is selected from the group consisting of phenyl, benzyl, pyridinyl, thiazolyl, dioxolanyl and tetrazolyl.

20 3. The compound of claim 2 and the pharmaceutically acceptable salts and esters thereof wherein:

R³ is selected from -C₁₋₂alkyl optionally substituted with fluoro and cyclopropyl;

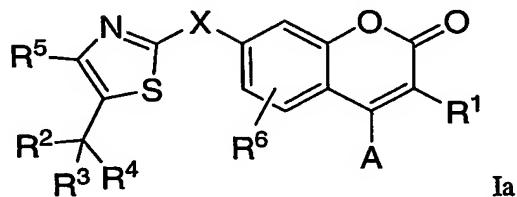
R⁴ is selected from -C₁₋₂alkyl optionally substituted with fluoro, cyclopropyl and Z;

25 A is unsubstituted, mono- or di-substituted and is selected from the group consisting of thienyl, furanyl, oxazolyl, thiazolyl, tetrazolyl, pyridinyl and phenyl; and

Z is unsubstituted, mono- or di-substituted and is selected from the group consisting of phenyl, pyridinyl and thiazolyl.

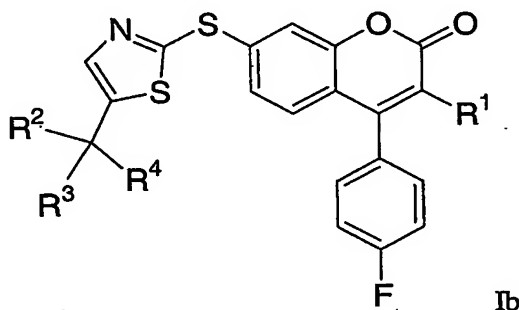
30 4. The compound of claim 3 and the pharmaceutically acceptable salts and esters thereof wherein: R¹ is selected from -H and -CH₃; R² is selected from -H and -OH; R³ is selected from -CF₃, -CH₃ and -C₂H₅ and cyclopropyl; R⁴ is selected from -CF₃, -CH₃ and -C₂H₅ and cyclopropyl; R⁵ is -H; R⁶ is -H; and A is selected from phenyl, 3-fluorophenyl, 4-fluoro-phenyl, unsubstituted or mono-substituted thiazolyl, and unsubstituted or mono-substituted pyridinyl.

5. The compound of claim 1 of structural Formula Ia:



and the pharmaceutically acceptable salts and esters thereof.

6. The compound of claim 1 of structural Formula Ib



and the pharmaceutically acceptable salts and esters thereof wherein:

R¹ is selected from the group consisting of -H and -CH₃;

R² is selected from the group consisting of -H and -OH;

R³ is selected from the group consisting of -CF₃ and -C₁₋₆alkyl optionally substituted with fluorine;

R⁴ is selected from the group consisting of -CF₃ and -C₁₋₆alkyl optionally substituted with fluorine;

or R³ and R⁴ are joined together with the carbon to which they are attached to form C₄₋₆cycloalkyl.

7. The compound of claim 1 selected from the group consisting of:

- 4-(4-fluorophenyl)-7-({5-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;
 4-phenyl-7-({5-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;
 4-pyridin-3-yl-7-({5-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;
 4-(2-methyl-1,3-thiazol-4-yl)-7-({5-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;
 4-(4-fluorophenyl)-7-({5-(1-hydroxycyclopentyl)-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;

4-(2-methyl-1,3-oxazol-4-yl)-7-({5-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;

4-(4-fluorophenyl)-7-({5-[1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;

5 4-(1,3-thiazol-4-yl)-7-({5-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;

(-)-7-({5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio)-4-(4-fluorophenyl)-2H-chromen-2-one;

0 (+)-7-({5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio)-4-(4-fluorophenyl)-2H-chromen-2-one;

7-({5-[(1S)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-phenyl-2H-chromen-2-one;

7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-phenyl-2H-chromen-2-one;

7-({5-[dicyclopropyl(hydroxy)methyl]-4-methyl-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-(dicyclopropylmethyl)-1,3-thiazol-2-yl}thio)-4-(4-fluorophenyl)-2H-chromen-2-one;

5 7-({5-(dicyclopropylmethyl)-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio)-4-(3-methylphenyl)-2H-chromen-2-one;

7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-(2-methyl-1,3-thiazol-4-yl)-2H-chromen-2-one;

10 7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-pyrimidin-5-yl-2H-chromen-2-one;

(-)-(R)-4-(4-fluorophenyl)-7-({5-[1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;

7-({5-[(1R)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-(3-methylphenyl)-2H-chromen-2-one;

25 (+)-7-({5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

(-)-7-({5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-[(1R)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

30 7-({5-[(1S)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

and the pharmaceutically acceptable salts and esters thereof.

8. The compound of claim 1 selected from the group consisting of:

(-)-(R)-4-(4-fluorophenyl)-7-({5-[1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-2H-chromen-2-one;

5 (+)-7-{{5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio}-4-pyridin-3-yl-2H-chromen-2-one;

(-)-7-{{5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio}-4-pyridin-3-yl-2H-chromen-2-one;

4-(4-fluorophenyl)-7-{{5-(1-hydroxycyclopentyl)-1,3-thiazol-2-yl}thio}-2H-chromen-2-one;

0 (-)-7-{{5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio}-4-(4-fluorophenyl)-2H-chromen-2-one;

(+)-7-{{5-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxyethyl)-1,3-thiazol-2-yl}thio}-4-(4-fluorophenyl)-2H-chromen-2-one;

7-({5-[(1S)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-phenyl-2H-chromen-2-one;

5 7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-phenyl-2H-chromen-2-one;

7-{{5-(dicyclopropylmethyl)-1,3-thiazol-2-yl}thio}-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-(2-methyl-1,3-thiazol-4-yl)-2H-chromen-2-one;

10 7-({5-[(1R)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-[(1S)-1-hydroxy-1-(trifluoromethyl)propyl]-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

7-({5-[dicyclopropyl(hydroxy)methyl]-1,3-thiazol-2-yl}thio)-4-pyridin-3-yl-2H-chromen-2-one;

and the pharmaceutically acceptable salts and esters thereof.

25

9. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

10. A method of preventing the synthesis, the action, or the release of leukotrienes in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.

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11. The method of claim 10 wherein the mammal is a human.

12. A method of treating asthma in a mammal comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 1.

13. A method of treating an inflammatory condition in a mammal which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 1.

14. A method of treating atherosclerosis comprising administering a therapeutically effective amount of a compound of claim 1 to a patient in need of such treatment.

15. A method for preventing or reducing the risk of developing atherosclerosis, comprising administering a prophylactically effective amount of a compound of claim 1 to a patient at risk for developing atherosclerosis.

16. A method for preventing or reducing the risk of an atherosclerotic disease event comprising administering a prophylactically effective amount of a compound of claim 1 to a patient at risk for having an atherosclerotic disease event.

17. A method for halting or slowing atherosclerotic plaque progression, comprising administering a therapeutically effective amount of a compound of claim 1 to a patient in need of such treatment.

18. A method for effecting regression of atherosclerotic plaque comprising administering a therapeutically effective amount of a compound of claim 1 to a patient in need of such treatment.

19. A method for preventing or reducing the risk of atherosclerotic plaque rupture comprising administering a prophylactically effective amount of a compound of claim 1 to a patient having atherosclerotic plaque.

20. A pharmaceutical composition comprised of a compound of claim 1 and a pharmaceutically acceptable carrier.

21. A pharmaceutical composition comprised of a compound of claim 1, a lipid altering compound and a pharmaceutically acceptable carrier.

22. Use of a compound of Formula I, as defined in any one of claims 1 to 8, or a pharmaceutically acceptable salt or ester thereof, in the manufacture of a medicament for preventing the synthesis, the action or the release of leukotrienes.

23. A compound of Formula I, as defined in any one of claims 1 to 8, or a pharmaceutically acceptable salt or ester thereof, for use in preventing the synthesis, the action or the release of leukotrienes.

24. A compound, salt or ester as defined in claim 23 for use in the treatment of a condition selected from the group consisting of asthma, inflammatory condition, and atherosclerosis.

25. A leukotriene biosynthesis inhibitor composition comprising an acceptable inhibitor amount of a composition of Formula 1, as defined in any one of claims 1 to 8, in association with a pharmaceutically acceptable carrier.

26. Use of an effective amount of a compound of any one of claims 1 to 8, for preventing the synthesis, the action, or the release of leukotrienes in a mammal.

27. Use of claim 26, wherein the mammal is a human.

28. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for treating asthma.

29. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for treating an inflammatory condition.

30. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for treating atherosclerosis.

31. Use of a prophylactically effective amount of a compound as defined in any one of claims 1 to 8, for preventing or reducing the risk of developing atherosclerosis.

32. Use of a prophylactically effective amount of a compound as defined in any one of claims 1 to 8, for preventing or reducing the risk of an atherosclerotic disease event.

33. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for altering or slowing atherosclerotic plaque progression.

34. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for effecting regression of atherosclerotic plaque.

35. Use of a prophylactically effective amount of a compound as defined in any one of claims 1 to 8, for preventing or reducing the risk of atherosclerotic plaque rupture.

5 36. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for treating asthma.

37. Use of a therapeutically effective amount of a compound as
10 defined in any one of claims 1 to 8, for the manufacture of a medicament, for treating an inflammatory condition.

38. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for
15 treating atherosclerosis.

39. Use of a prophylactically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for preventing or reducing the risk of developing atherosclerosis.

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40. Use of a prophylactically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for preventing or reducing the risk of an atherosclerotic disease event.

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41. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for altering or slowing atherosclerotic plaque progression.

42. Use of a therapeutically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for effecting regression of atherosclerotic plaque.

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43. Use of a prophylactically effective amount of a compound as defined in any one of claims 1 to 8, for the manufacture of a medicament, for preventing or reducing the risk of atherosclerotic plaque rupture.